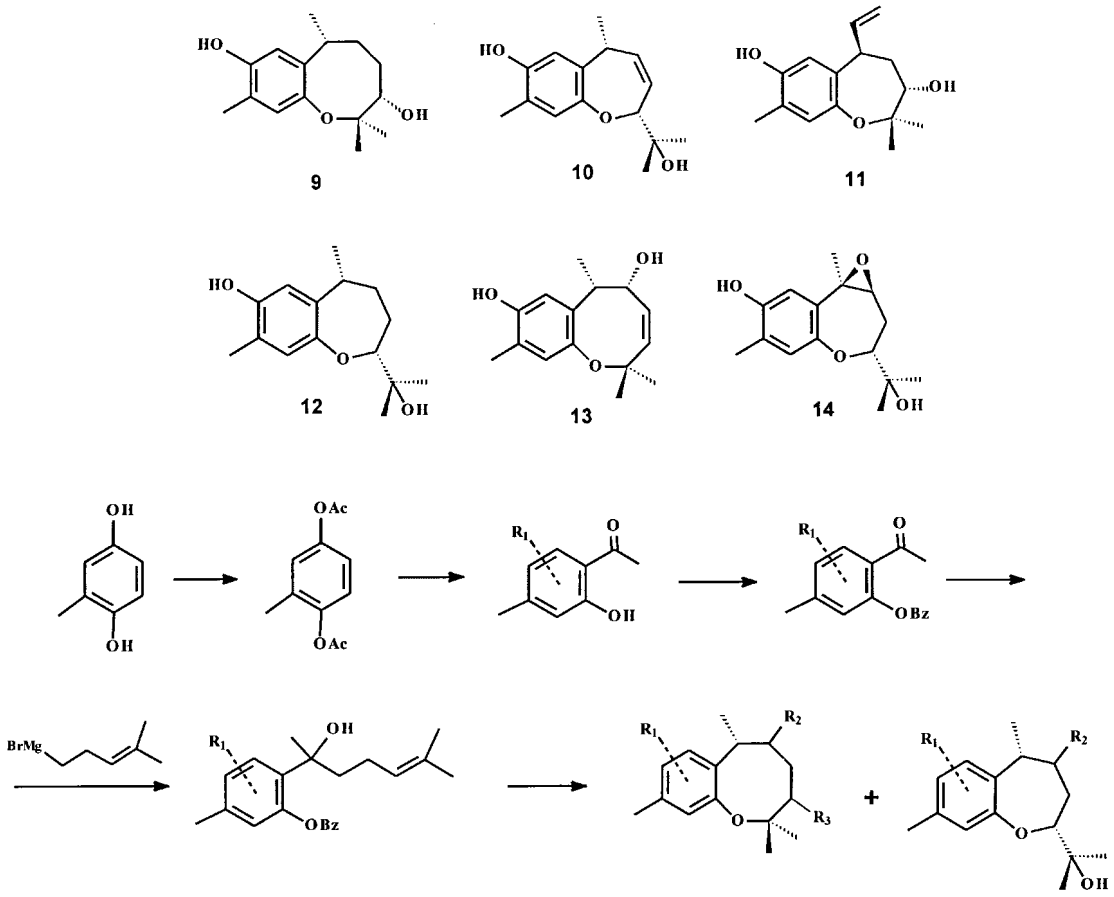

Figure 3. Synthesis routes for heliannuols.

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Interactions of picrodendrins and related terpenoids with ionotropic GABA receptors of mammals and insects

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Abstract: Different structural features govern the interaction of picrodendrins and related terpenoids with rat and with housefly GABA receptors. This supports previous studies which suggest that there are significant differences between the structures of the binding sites in these two receptors.

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	R_1	R_2	R_3	R_4
Picrodendrin-A:	H	OH	CH_2OH	OCH_3
-M:	OH	H	CH_3	OCH_3
-Q:	H	H	CH_3	OCH_3
-T:	H	OH	OCH_3	CH_2OH

	R_5	R_6	R_7	R_8	R_9
Picrodendrin-E:	OH	H	OH	H	OH
-F:	H	OH	OH	OH	OH
-L:	H	OH	H	OH	OH
-O:	H	H	OH	H	OH

Figure 1. Structures of picrodendrins.

Keywords: picrodendrin; terpenoid; structure–activity relationship; ionotropic GABA receptor; noncompetitive antagonist; binding site

Naturally occurring, biologically active compounds provide valuable tools for elucidating the molecular basis of physiological events. In the present study, 28 picrotoxane terpenoids, including picrodendrins (Fig 1)[1,2] isolated from the Euphorbiaceae plant, *Picrodendron baccatum* (L) Krug & Urban, have been evaluated for their ability to inhibit specific binding of [^{3}H]1-(4-ethynylphenyl)-4-propyl-2,6,7-trioxabicyclo[2.2.2.]octane (EBOB), the noncompetitive antagonist of ionotropic GABA receptors, to rat-brain and housefly-head membranes.[3] Picrodendrin Q was the most potent competitive inhibitor, with IC_{50} values of 16nM (rat) and 22nM (houseflies). The spiro γ-butyrolactone moiety, containing a carbonyl group conjugated with an unsaturated bond at the 13-position and the hydrophobic substituents at the 4-position play important roles in the interaction of picrodendrins with their binding site in rat GABA receptors. In contrast, such structural features are not strictly required in the case of the interaction with housefly GABA receptors; the spiro γ-butyrolactone, bearing the 16-sp^3 carbon atom at the 13-position and hydroxyl groups at various positions are somewhat tolerated.

Quantitative structure–activity studies have clearly shown that the electronegativity of the 16-carbon atom and the presence or absence of the 4- and 8-hydroxyl groups are important determinants of potency of norditerpenes in housefly receptors, while the negative charge on the 17-carbonyl oxygen atom is likely to be important in the case of rat receptors. These findings are consistent with those of our previous studies[4] that there are significant differences in the structures of their binding site between rat and housefly GABA receptors.

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Insecticidal toxins from the bacterium *Photorhabdus luminescens*: gene cloning and toxin histopathology

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Abstract: Four toxin complexes, Tca, Tcb, Tcc and Tcd from the culture broth of *Photorhabdus luminescens* have been purified and the four toxin complex encoding loci, *tca, tcb, tcc* and *tcd*, cloned. Genetic knockout of either *tca* or *tcd* reduced oral toxicity to *Manduca sexta*, and knockout of both loci eliminated activity. Purified Tca specifically affected the insect midgut, despite its putative normal delivery directly into the insect haemocel. These *Photorhabdus* toxins may form useful alternatives to other orally active bacterial protein toxins such as those from *Bacillus thuringiensis*.

Keywords: *Photorhabdus luminescens*; bacterial toxins; toxin complexes; insecticidal activity

Photorhabdus luminescens (Enterobacteriaceae) inhabits

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